

tetrahydrofolic acid, 5-formimino-(6S)-tetrahydrofolic acid, and polyglutamyl derivatives thereof; and

a nutritional substance for human consumption selected from the group consisting of a food preparation, an essential nutrient preparation, and combinations thereof;

wherein the total amount of said one or more natural isomers of reduced folate in said composition is between about 5% and about 200% of a human daily requirement for folate per customarily consumed quantity of said composition;

B1
wherein, when the nutritional substance is a food preparation, the food preparation comprises two or more food components and each gram of said food preparation has a natural molar amount, N, of said one or more natural isomers of reduced folate, wherein N is greater or equal to zero and wherein each gram of said composition has a total molar amount, T, of said one or more natural isomers of reduced folate greater than N; [and]

wherein, when the nutritional substance is an essential nutrient preparation, the essential nutrient preparation comprises a vitamin other than ascorbic acid; and

wherein, when the nutritional substance is an essential nutrient preparation and when said composition comprises an amount of 5-formyl-(6S)-tetrahydrofolic acid, said composition further comprises no 5-formyl-(6R)-tetrahydrofolic acid, or, if present, said composition further comprises 5-formyl-(6R)-tetrahydrofolic acid in an amount less than the amount of 5-formyl-(6S)-tetrahydrofolic acid present in said composition.

230. (Amended) A composition for human consumption comprising:

B2
one or more natural isomers of reduced folate selected from the group consisting of (6S)-tetrahydrofolic acid, 5-methyl-(6S)-tetrahydrofolic acid, 5-formyl-(6S)-tetrahydrofolic acid, 10-formyl-(6R)-tetrahydrofolic acid,

5,10-methylene-(6R)-tetrahydrofolic acid, 5,10-methenyl-(6R)-tetrahydrofolic acid, 5-formimino-(6S)-tetrahydrofolic acid, and polyglutamyl derivatives thereof; and

a nutritional substance for human consumption selected from the group consisting of a food preparation, an essential nutrient preparation, and combinations thereof;

wherein the total amount of said one or more natural isomers of reduced folate in said composition is less than or equal to about 4.5 micromoles per customarily consumed quantity of said composition;

B2
wherein, when the nutritional substance is a food preparation, the food preparation comprises two or more food components and each gram of said food preparation has a natural molar amount, N, of said one or more natural isomers of reduced folate, wherein N is greater or equal to zero and wherein each gram of said composition has a total molar amount, T, of said one or more natural isomers of reduced folate greater than N; [and]

wherein, when the nutritional substance is an essential nutrient preparation; the essential nutrient preparation comprises a vitamin other than ascorbic acid; and

wherein, when the nutritional substance is an essential nutrient preparation and when said composition comprises an amount of 5-formyl-(6S)-tetrahydrofolic acid, said composition further comprises no 5-formyl-(6R)-tetrahydrofolic acid, or, if present, said composition further comprises 5-formyl-(6R)-tetrahydrofolic acid in an amount less than the amount of 5-formyl-(6S)-tetrahydrofolic acid present in said composition.

B3
28
9. (Amended) A method for increasing the folate content of a nutritional substance for human consumption comprising:
providing a nutritional substance for human consumption selected from the group consisting of a food preparation, an essential nutrient preparation, and combinations thereof; and

incorporating into the nutritional substance an amount of one or more natural isomers of reduced folate selected from the group consisting of (6S)-tetrahydrofolic acid, 5-methyl-(6S)-tetrahydrofolic acid, 5-formyl-(6S)-tetrahydrofolic acid, 10-formyl-(6R)-tetrahydrofolic acid, 5,10-methylene-(6R)-tetrahydrofolic acid, 5,10-methenyl-(6R)-tetrahydrofolic acid, 5-formimino-(6S)-tetrahydrofolic acid, and polyglutamyl derivatives thereof, thereby forming a composition;

wherein the total amount of said one or more natural isomers of reduced folate incorporated into said nutritional substance is between about 5% and about 200% of a human daily requirement for folate per customarily consumed quantity of said nutritional substance;

B3
wherein, when the nutritional substance is a food preparation, the food preparation comprises two or more food components and each gram of said food preparation has a natural molar amount, N, of said one or more natural isomers of reduced folate, wherein N is greater or equal to zero and wherein each gram of said composition has a total molar amount, T, of said one or more natural isomers of reduced folate greater than N; [and]

wherein, when the nutritional substance is an essential nutrient preparation, the essential nutrient preparation comprises a vitamin other than ascorbic acid; and

wherein, when the nutritional substance is an essential nutrient preparation and when the composition comprises an amount of 5-formyl-(6S)-tetrahydrofolic acid, the composition further comprises no 5-formyl-(6R)-tetrahydrofolic acid, or, if present, the composition further comprises 5-formyl-(6R)-tetrahydrofolic acid in an amount less than the amount of 5-formyl-(6S)-tetrahydrofolic acid present in the composition.

1052. (Once Amended) A method for increasing the folate content of a nutritional substance for human consumption comprising:

providing a nutritional substance for human consumption selected from the group consisting of a food preparation, an essential nutrient preparation, and combinations thereof; and incorporating into the nutritional substance an amount of one or more natural isomers of reduced folate selected from the group consisting of (6S)-tetrahydrofolic acid, 5-methyl-(6S)-tetrahydrofolic acid, 5-formyl-(6S)-tetrahydrofolic acid, 10-formyl-(6R)-tetrahydrofolic acid, 5,10-methylene-(6R)-tetrahydrofolic acid, 5,10-methenyl-(6R)-tetrahydrofolic acid, 5-formimino-(6S)-tetrahydrofolic acid, and polyglutamyl derivatives thereof, thereby forming a composition;

by wherein the total amount of said one or more natural isomers of reduced folate in said composition is less than or equal to about 4.5 micromoles per customarily consumed quantity of said composition;

wherein, when the nutritional substance is a food preparation, the food preparation comprises two or more food components and each gram of said food preparation has a natural molar amount, N, of said one or more natural isomers of reduced folate, wherein N is greater or equal to zero and wherein each gram of said composition has a total molar amount, T, of said one or more natural isomers of reduced folate greater than N; [and]

wherein, when the nutritional substance is an essential nutrient preparation, the essential nutrient preparation comprises a vitamin other than ascorbic acid; and

wherein, when the nutritional substance is an essential nutrient preparation and when the composition comprises an amount of 5-formyl-(6S)-tetrahydrofolic acid, the composition further comprises no 5-formyl-(6R)-tetrahydrofolic acid, or, if present, the composition further comprises 5-formyl-(6R)-

B4
tetrahydrofolic acid in an amount less than the amount of 5-formyl-(6S)-tetrahydrofolic acid present in the composition.

Per. (Amended) A composition for consumption by an animal, the animal selected from the group consisting of dog, cat, poultry, cattle, goat, horse, mink, fox, and sheep, the composition comprising:

one or more natural isomers of reduced folate selected from the group consisting of (6S)-tetrahydrofolic acid, 5-methyl-(6S)-tetrahydrofolic acid, 5-formyl-(6S)-tetrahydrofolic acid, 10-formyl-(6R)-tetrahydrofolic acid, 5,10-methylene-(6R)-tetrahydrofolic acid, 5,10-methenyl-(6R)-tetrahydrofolic acid, 5-formimino-(6S)-tetrahydrofolic acid, and polyglutamyl derivatives thereof; and

B5
a nutritional substance for consumption by the animal selected from the group consisting of a food preparation, an essential nutrient preparation, and combinations thereof;

wherein the total amount of said one or more natural isomers of reduced folate in said composition is between about 5% and about 3000% of an animal daily requirement for folate per customarily consumed quantity of said composition;

wherein, when the nutritional substance is a food preparation, the food preparation comprises two or more food components and each gram of said food preparation has a natural molar amount, N, of said one or more natural isomers of reduced folate, wherein N is greater or equal to zero and wherein each gram of said composition has a total molar amount, T, of said one or more natural isomers of reduced folate greater than N; [and]

wherein, when the nutritional substance is an essential nutrient preparation, the essential nutrient preparation comprises a vitamin other than ascorbic acid; and

wherein, when the nutritional substance is an essential nutrient preparation and when said composition comprises an

B5 amount of 5-formyl-(6S)-tetrahydrofolic acid, said composition further comprises no 5-formyl-(6R)-tetrahydrofolic acid, or, if present, said composition further comprises 5-formyl-(6R)-tetrahydrofolic acid in an amount less than the amount of 5-formyl-(6S)-tetrahydrofolic acid present in said composition.

Amended. (Amended) A method for increasing the folate content of a nutritional substance for consumption by an animal, the animal selected from the group consisting of dog, cat, poultry, cattle, goat, horse, mink, fox, and sheep, the method comprising:

providing a nutritional substance for consumption by the animal selected from the group consisting of a food preparation, an essential nutrient preparation, and combinations thereof; and

B6 incorporating into the nutritional substance an amount of one or more natural isomers of reduced folate selected from the group consisting of (6S)-tetrahydrofolic acid, 5-methyl-(6S)-tetrahydrofolic acid, 5-formyl-(6S)-tetrahydrofolic acid, 10-formyl-(6R)-tetrahydrofolic acid, 5,10-methylene-(6R)-tetrahydrofolic acid, 5,10-methenyl-(6R)-tetrahydrofolic acid, 5-formimino-(6S)-tetrahydrofolic acid, and polyglutamyl derivatives thereof, thereby forming a composition;

wherein the total amount of said one or more natural isomers of reduced folate incorporated into said nutritional substance is between about 5% and about 3000% of an animal daily requirement for folate per customarily consumed quantity of said nutritional substance;

wherein, when the nutritional substance is a food preparation, the food preparation comprises two or more food components and each gram of said food preparation has a natural molar amount, N, of said one or more natural isomers of reduced folate, wherein N is greater or equal to zero and wherein each gram of said composition has a total molar

amount, T, of said one or more natural isomers of reduced folate greater than N; [and]

wherein, when the nutritional substance is an essential nutrient preparation, the essential nutrient preparation comprises a vitamin other than ascorbic acid; and

B6 wherein, when the nutritional substance is an essential nutrient preparation and when the composition comprises an amount of 5-formyl-(6S)-tetrahydrofolic acid, the composition further comprises no 5-formyl-(6R)-tetrahydrofolic acid, or, if present, the composition further comprises 5-formyl-(6R)-tetrahydrofolic acid in an amount less than the amount of 5-formyl-(6S)-tetrahydrofolic acid present in the composition.

Please add new claims 83-111 as follows:

583. A composition according to claim ⁴52, wherein the one or more natural isomers of reduced folate is 5-methyl-(6S)-tetrahydrofolic acid or a polyglutamyl derivative thereof.

⁶84. A composition according to claim ⁴52, wherein the one or more natural isomers of reduced folate is 5-formyl-(6S)-tetrahydrofolic acid or a polyglutamyl derivative thereof.

B7 ¹²⁵85. A composition according to claim ⁴52, wherein the one or more natural isomers of reduced folate is 5,10-methenyl-(6R)-tetrahydrofolic acid or a polyglutamyl derivative thereof.

86. A method according to claim 62, wherein, when the nutritional substance is an essential nutrient preparation and when the composition comprises an amount of 5-formyl-(6S)-tetrahydrofolic acid, the composition further comprises no 5-formyl-(6R)-tetrahydrofolic acid, or, if present, the composition further comprises 5-formyl-(6R)-tetrahydrofolic

acid in an amount less than the amount of 5-formyl-(6S)-tetrahydrofolic acid present in the composition.

²¹
P. 27. A method according to claim ²⁵~~25~~, wherein the one or more natural isomers of reduced folate is 5-methyl-(6S)-tetrahydrofolic acid or a polyglutamyl derivative thereof.

¹³
P. 28. A method according to claim ²⁵~~25~~, wherein the one or more natural isomers of reduced folate is 5-formyl-(6S)-tetrahydrofolic acid or a polyglutamyl derivative thereof.

¹⁴
P. 29. A method according to claim ²⁵~~25~~, wherein the one or more natural isomers of reduced folate is 5,10-methenyl-(6R)-tetrahydrofolic acid or a polyglutamyl derivative thereof.

²²
B7 P. 30. A composition according to claim ²¹~~21~~, wherein the one or more natural isomers of reduced folate is 5-methyl-(6S)-tetrahydrofolic acid or a polyglutamyl derivative thereof.

²³
P. 31. A composition according to claim ²¹~~21~~, wherein the one or more natural isomers of reduced folate is 5-formyl-(6S)-tetrahydrofolic acid or a polyglutamyl derivative thereof.

²⁴
P. 32. A composition according to claim ²¹~~21~~, wherein the one or more natural isomers of reduced folate is 5,10-methenyl-(6R)-tetrahydrofolic acid or a polyglutamyl derivative thereof.

³¹
³⁰
P. 33. A method according to claim ²⁵~~25~~, wherein the one or more natural isomers of reduced folate is 5-methyl-(6S)-tetrahydrofolic acid or a polyglutamyl derivative thereof.

³⁰
~~34~~ A method according to claim ~~30~~³⁰, wherein the one or more natural isomers of reduced folate is 5-formyl-(6S)-tetrahydrofolic acid or a polyglutamyl derivative thereof.

³⁰
~~35~~ A method according to claim ~~30~~³⁰, wherein the one or more natural isomers of reduced folate is 5,10-methenyl-(6R)-tetrahydrofolic acid or a polyglutamyl derivative thereof.

³⁵
~~36~~ A method of increasing a human subject's dietary intake of folate comprising administering to the human subject a composition comprising:

one or more natural isomers of reduced folate selected from the group consisting of (6S)-tetrahydrofolic acid, 5-methyl-(6S)-tetrahydrofolic acid, 5-formyl-(6S)-tetrahydrofolic acid, 10-formyl-(6R)-tetrahydrofolic acid, 5,10-methylene-(6R)-tetrahydrofolic acid, 5,10-methenyl-(6R)-tetrahydrofolic acid, 5-formimino-(6S)-tetrahydrofolic acid, and polyglutamyl derivatives thereof; and

a nutritional substance for human consumption selected from the group consisting of a food preparation, an essential nutrient preparation, and combinations thereof;

wherein the total amount of said one or more natural isomers of reduced folate in said composition is between about 5% and about 200% of a human daily requirement for folate per customarily consumed quantity of said composition;

wherein, when the nutritional substance is a food preparation, the food preparation comprises two or more food components and each gram of said food preparation has a natural molar amount, N, of said one or more natural isomers of reduced folate, wherein N is greater or equal to zero and wherein each gram of said composition has a total molar amount, T, of said one or more natural isomers of reduced folate greater than N; and

wherein, when the nutritional substance is an essential nutrient preparation, the essential nutrient preparation comprises a vitamin other than ascorbic acid.

Sub c8
97. A method of increasing a human subject's dietary intake of folate comprising administering to the human subject a composition according to claim 46.

98. A method of increasing a human subject's dietary intake of folate comprising administering to the human subject a composition according to claim 49.

B7
99. A method of increasing a human subject's dietary intake of folate comprising administering to the human subject a composition comprising:

one or more natural isomers of reduced folate selected from the group consisting of (6S)-tetrahydrofolic acid, 5-methyl-(6S)-tetrahydrofolic acid, 5-formyl-(6S)-tetrahydrofolic acid, 10-formyl-(6R)-tetrahydrofolic acid, 5,10-methylene-(6R)-tetrahydrofolic acid, 5,10-methenyl-(6R)-tetrahydrofolic acid, 5-formimino-(6S)-tetrahydrofolic acid, and polyglutamyl derivatives thereof; and

a nutritional substance for human consumption selected from the group consisting of a food preparation, an essential nutrient preparation, and combinations thereof;

wherein the total amount of said one or more natural isomers of reduced folate in said composition is less than or equal to about 4.5 micromoles per customarily consumed quantity of said composition;

wherein, when the nutritional substance is a food preparation, the food preparation comprises two or more food components and each gram of said food preparation has a natural molar amount, N, of said one or more natural isomers of reduced folate, wherein N is greater or equal to zero and

wherein each gram of said composition has a total molar amount, T, of said one or more natural isomers of reduced folate greater than N; and

wherein, when the nutritional substance is an essential nutrient preparation, the essential nutrient preparation comprises a vitamin other than ascorbic acid.

³⁹
100. A method according to claim ³⁵ 36, ³⁶ 37, ³⁷ 38, or ³⁸ 39, wherein said administering is carried out by enteral administration.

⁴⁰
101. A method according to claim ³⁵ 36, ³⁶ 37, ³⁷ 38, or ³⁸ 39, wherein the human is selected from the group consisting of a pregnant female; a female who has had a miscarriage; a female who has carried a fetus having a neural tube defect, a cleft lip defect, or a cleft palate defect; and a human who suffers vascular disease.

⁴¹
102. A method according to claim ³⁵ 36, ³⁶ 37, or ³⁷ 38, wherein, when the nutritional substance is an essential nutrient preparation and when said composition comprises an amount of 5-formyl-(6S)-tetrahydrofolic acid, said composition further comprises no 5-formyl-(6R)-tetrahydrofolic acid, or, if present, said composition further comprises 5-formyl-(6R)-tetrahydrofolic acid in an amount less than the amount of 5-formyl-(6S)-tetrahydrofolic acid present in said composition.

⁴²
103. A method of increasing an animal subject's dietary intake of folate, the animal selected from the group consisting of dog, cat, poultry, cattle, goat, horse, mink, fox, and sheep, the method comprising administering to the animal subject a composition comprising:

one or more natural isomers of reduced folate selected from the group consisting of (6S)-tetrahydrofolic acid, 5-

methyl-(6S)-tetrahydrofolic acid, 5-formyl-(6S)-tetrahydrofolic acid, 10-formyl-(6R)-tetrahydrofolic acid, 5,10-methylene-(6R)-tetrahydrofolic acid, 5,10-methenyl-(6R)-tetrahydrofolic acid, 5-formimino-(6S)-tetrahydrofolic acid, and polyglutamyl derivatives thereof; and

a nutritional substance for consumption by the animal selected from the group consisting of a food preparation, an essential nutrient preparation, and combinations thereof;

wherein the total amount of said one or more natural isomers of reduced folate in said composition is between about 5% and about 3000% of an animal daily requirement for folate per customarily consumed quantity of said composition;

57 wherein, when the nutritional substance is a food preparation, the food preparation comprises two or more food components and each gram of said food preparation has a natural molar amount, N, of said one or more natural isomers of reduced folate, wherein N is greater or equal to zero and wherein each gram of said composition has a total molar amount, T, of said one or more natural isomers of reduced folate greater than N; and

wherein, when the nutritional substance is an essential nutrient preparation, the essential nutrient preparation comprises a vitamin other than ascorbic acid.

104. A method of increasing an animal subject's dietary intake of folate, the animal selected from the group consisting of dog, cat, poultry, cattle, goat, horse, mink, fox, and sheep, the method comprising administering to the animal subject a composition according to claim 68.

105. A method of increasing an animal subject's dietary intake of folate, the animal selected from the group consisting of dog, cat, poultry, cattle, goat, horse, mink,

fox, and sheep, the method comprising administering to the animal subject a composition according to claim 69.

sub ca) 106. A method according to claim 103, 104, or 105, wherein said administering is carried out by enteral administration.

B7 107. A method according to claim 103 or 105, wherein, when the nutritional substance is an essential nutrient preparation and when said composition comprises an amount of 5-formyl-(6S)-tetrahydrofolic acid, said composition further comprises no 5-formyl-(6R)-tetrahydrofolic acid, or, if present, said composition further comprises 5-formyl-(6R)-tetrahydrofolic acid in an amount less than the amount of 5-formyl-(6S)-tetrahydrofolic acid present in said composition.

108. A composition according to claim 49, wherein, when said composition comprises an amount of 5-formyl-(6S)-tetrahydrofolic acid, said composition further comprises no 5-formyl-(6R)-tetrahydrofolic acid, or, if present, said composition further comprises 5-formyl-(6R)-tetrahydrofolic acid in an amount less than the amount of 5-formyl-(6S)-tetrahydrofolic acid present in said composition.

109. A method according to claim 56, wherein said incorporating the one or more natural isomers of reduced folate into the nutritional substance forms a composition and wherein, when the composition comprises an amount of 5-formyl-(6S)-tetrahydrofolic acid, the composition further comprises no 5-formyl-(6R)-tetrahydrofolic acid, or, if present, the composition further comprises 5-formyl-(6R)-tetrahydrofolic acid in an amount less than the amount of 5-formyl-(6S)-tetrahydrofolic acid present in the composition.

B

110. A composition according to claim 69, wherein, when said composition comprises an amount of 5-formyl-(6S)-tetrahydrofolic acid, said composition further comprises no 5-formyl-(6R)-tetrahydrofolic acid, or, if present, said composition further comprises 5-formyl-(6R)-tetrahydrofolic acid in an amount less than the amount of 5-formyl-(6S)-tetrahydrofolic acid present in said composition.

B7
111. A method according to claim 75, wherein said incorporating the one or more natural isomers of reduced folate into the nutritional substance forms a composition and wherein, when the composition comprises an amount of 5-formyl-(6S)-tetrahydrofolic acid, the composition further comprises no 5-formyl-(6R)-tetrahydrofolic acid, or, if present, the composition further comprises 5-formyl-(6R)-tetrahydrofolic acid in an amount less than the amount of 5-formyl-(6S)-tetrahydrofolic acid present in the composition.

Respectfully submitted,

Dated: January 13, 1999

Peter Rogalsky
Peter Rogalsky
Registration No. 38,601

Braman & Rogalskyj, LLP
P.O. Box 352
Canandaigua, New York 14424-0352
Telephone: (716) 393-3004
Facsimile: (716) 393-3001

Certificate of Mailing - 37 CFR 1.8 (a)

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner of Patents and Trademarks, Washington, D.C. 20231 on the date below.

1/13/99
Date

Peter Rogalsky
Peter Rogalsky